1: J Immunol Methods 1994 Apr 15;170(2):261-8 Related Articles, Links

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Production and characterization of monoclonal antibodies specific for the murine T cell receptor zeta chain.

van Oers NS, Teh SJ, Irving BA, Tiong J, Weiss A, Teh HS.

Howard Hughes Medical Institute, San Francisco, CA 94143-0724.

PubMed Services

The T cell receptor (TCR) comprises an antigen-specific alpha beta heterodimer non-covalently associated with the CD3 gamma delta epsilon and TCR zeta subunits. Both the CD3 and TCR zeta subunits are proposed to be responsible for the intracellular signal-transduction events. We report here the production of eight monoclonal antibodies (mAbs) that bind in an ELISA assay to a 113 amino acid synthetic peptide corresponding to the cytoplasmic domain of TCR zeta. Western blot analysis of anti-CD8 precipitates of lysates of transfectants expressing chimeric CD8/zeta constructs encoding increasing COOH-terminal truncations of TCR zeta indicates that four of these mAbs recognized the region of TCR zeta chain comprising the last 29 COOH-terminal residues. Thus, this region of TCR theta may encode an immunodominant epitope. Furthermore, one of these mAbs, G3, is capable of precipitating both non-phosphorylated and tyrosine phosphorylated TCR zeta. The G3 mAb should be useful for elucidating the structural and signalling characteristics of the TCR zeta chain.

Related Resources

PMID: 7512608 [PubMed - indexed for MEDLINE]

1: Blood 1996 Jul 1;88(1):236-41

T cells from patients with Hodgkin's disease have a defective T-cell receptor zeta chain expression that is reversible by T-cell stimulation with CD3 and CD28.

Renner C, Ohnesorge S, Held G, Bauer S, Jung W, Pfitzenmeier JP, Pfreundschuh M.

Medical Department I, University of the Saarland, Homburg, Germany.

To investigate the mechanisms underlying the deficiency of T lymphocytes from patients with Hodgkin's disease, we investigated the expression of the T-cell receptor (TCR) zeta chain in patients with Hodgkin's disease. By flow cytometry using an anti-zeta chain monoclonal antibody, peripheral blood T lymphocytes from patients with untreated Hodgkin's disease were shown to express decreased levels of the TCR zeta chain. After stimulation by combined CD3 and CD28 cross-linking, T cells from Hodgkin's disease patients upregulated zeta chain protein expression to normal values within 48 hours and achieved a cytolytic potential and levels of interleukin (IL)-2 secretion that were not different from T cells obtained from healthy controls. These results show that downregulation of the TCR zeta chain in Hodgkin's T lymphocytes is a reversible event. Costimulation of CD3 and CD28 is a novel approach for overcoming the T-cell deficiency in Hodgkin's disease and might be exploited clinically. As upregulation of the zeta chain can also be achieved using bispecific monoclonal antibodies (BI-MoAbs) with specificity for tumor antigens and CD3 and CD28, respectively, an immunotherapy with CD3/CD30 and CD28/CD30 Bi-MoAbs may overcome and should therefore, not be jeopardized by the inherent T-cell deficiency in patients with Hodgkin's disease.

PMID: 8704179 [PubMed - indexed for MEDLINE]

1: AAA40900. T-cell receptor z...[gi:203386] BLink, Links

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LOCUS       AAA40900                 164 aa            linear   ROD 22-JUL-1993
DEFINITION  T-cell receptor zeta chain.
ACCESSION   AAA40900
VERSION     AAA40900.1  GI:203386
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KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae;
            Rattus.
REFERENCE   1  (residues 1 to 164)
  AUTHORS   Farber,D.L., Giorda,R., Nettleton,M.Y., Trucco,M., Kochan,J.P. and
            Sears,D.W.
  TITLE     Rat class III Fc gamma receptor isoforms differ in IgG
            subclass-binding specificity and fail to associate productively
            with rat CD3 zeta
  JOURNAL   J. Immunol. 150 (10), 4364-4375 (1993)
  MEDLINE   93246650
   PUBMED   8482840
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Revised: August 5, 2002.

☐1: A44266. protein-tyrosine ...[gi:346421] BLink, Domains, Links

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DEFINITION  protein-tyrosine kinase (EC 2.7.1.112) ZAP-70 - human.
ACCESSION   A44266
VERSION     A44266  GI:346421
DBSOURCE    pir: locus A44266;

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            genetic: #gene GDB:SRK; ZAP-70 ##cross-references GDB:433738;
            OMIM:176947 #map_position 4pter-4qter #note defects in this gene
            are associated with an autosomal recessive form of severe combined
            immunodeficienc (SCID)
            ;
            superfamily: protein-tyrosine kinase ZAP-70; protein kinase
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            ;
            PIR dates: 10-Jun-1993 #sequence_revision 18-Nov-1994 #text_change
            19-Dec-1997
            .
KEYWORDS    ATP; phosphotransferase; severe combined immunodeficiency; T-cell;
            tyrosine-specific protein kinase.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 619)
  AUTHORS   Chan,A.C., Iwashima,M., Turck,C.W. and Weiss,A.
  TITLE     ZAP-70: a 70 kd protein-tyrosine kinase that associates with the
            TCR zeta chain
  JOURNAL   Cell 71 (4), 649-662 (1992)
  MEDLINE   93046663
   PUBMED   1423621
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      241 lkadgliycl keacpnssas nasgaaaptl pahpstlthp qrridtlnsd gytpeparit
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Revised: August 5, 2002.

☐1: CAC41082. T cell receptor i...[gi:14330720] BLink, Links

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LOCUS       CAC41082                187 aa            linear   ROD 06-JUN-2001
DEFINITION  T cell receptor interacting molecule [Mus musculus].
ACCESSION   CAC41082
VERSION     CAC41082.1  GI:14330720
DBSOURCE    embl locus MMU297969, accession AJ297969.1
KEYWORDS    .
SOURCE      Mus musculus (house mouse)
  ORGANISM  Mus musculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
REFERENCE   1
  AUTHORS   Kirchgessner,H., Dietrich,J., Scherer,J., Isomaki,P., Korinek,V.,
            Hilgert,I., Bruyns,E., Leo,A., Cope,A.P. and Schraven,B.
  TITLE     The transmembrane adaptor protein TRIM regulates T cell receptor
            (TCR) expression and TCR-mediated signaling via an association with
            the TCR zeta chain
  JOURNAL   J. Exp. Med. 193 (11), 1269-1284 (2001)
  MEDLINE   21286433
   PUBMED   11390434
REFERENCE   2  (residues 1 to 187)
  AUTHORS   Bruyns,E.
  TITLE     Direct Submission
  JOURNAL   Submitted (21-NOV-2000) Bruyns E., Immunology, University of
            Heidelberg, Im Neuenheimer Feld 305, 69120 Heidelberg, GERMANY
COMMENT     Related sequence AJ224878.
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                     /strain="C57/Bl6"
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                     /tissue_type="spleen"
                     /dev_stage="adult"
     Protein         1..187
                     /product="T cell receptor interacting molecule"
                     /function="unknown"
     CDS             1..187
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                     /coded_by="AJ297969.1:55..618"
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      121 krrrprkqnt nvsdrgkdtq vytmdanvsq inmvesfppd nqvveesihd dparlfglir
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//
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Revised: August 5, 2002.

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NEWS 20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 23	Sep 03	JAPIO has been reloaded and enhanced
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NEWS 38	Dec 30	ISMEC no longer available
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NEWS 40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
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NEWS 42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 43	Feb 13	CANCERLIT is no longer being updated
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=> s zeta chain
L1 4147 ZETA CHAIN

=> s l1 and antibody
L2 1106 L1 AND ANTIBODY

=> s l2 and rat zeta chain
L3 1 L2 AND RAT ZETA CHAIN

=> d l3 cbib abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
2000:53887 Document No. 132:106967 Immunological reagent specifically interacting with the extracellular domain of the human **zeta**

chain. Reiter, Christian (Connex G.m.b.H., Germany). PCT Int. Appl. WO 2000003016 A1 20000120, 79 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP4838 19990709. PRIORITY: EP 1998-112867 19980710.

AB The present invention relates to a nucleic acid mol. comprising a nucleic acid sequence encoding at least one complementary detg. region (CDR) of a variable region of an **antibody**, said **antibody** specifically interacting with the extracellular domain of the human **zeta-chain**, said **antibody** being obtainable by immunizing a rat with Jurkat cells and subsequently with a conjugate comprising a carrier mol. and a peptide comprising the 11 N-terminal amino acids of the **rat zeta-chain**. Preferably, the (poly)peptide encoded by the nucleic acid mol. of the invention is a monospecific or bispecific **antibody**. The invention also relates to pharmaceutical compns. comprising i.a. the nucleic acid mol. or **antibody** of the invention as well as to kits comprising the aforementioned compds. Finally, the invention relates to a method for the detn. of **zeta-chain** or eta-chain expression on NK-cells, T-cells or precursors thereof employing the **antibody** of the invention. The **antibodies** are useful for treatment and prevention of autoimmune diseases, immune deficiency, T cell malignancies, infectious diseases, and for suppression of immune response to avoid graft rejection after organ transplant.

```
=> s l1 and rat
L4          100 L1 AND RAT

=> s l4 and antibody
L5           39 L4 AND ANTIBODY

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PROCESSING COMPLETED FOR L5
L6           25 DUP REMOVE L5 (14 DUPLICATES REMOVED)

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'CIB' IS NOT A VALID FORMAT
In a multifile environment, a format can only be used if it is valid
in at least one of the files.  Refer to file specific help messages
or the STNGUIDE file for information on formats available in
individual files.
REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT):ab

L6   ANSWER 1 OF 25  CAPLUS  COPYRIGHT 2003 ACS
```

AB The MRC OX52 monoclonal **antibody** is a marker of **rat** T lymphocytes. The authors have cloned by polymerase chain reaction the **rat** homolog of CD6, and fluorescein-activated cell sorter anal. and immunopptns. using OX52 in COS7 cells transfected with **rat** CD6 cDNA showed that CD6 is the cell-surface mol. recognized by OX52. Immunopptn. anal. showed that CD6 copptd. with CD5, which in turn, was copptd. equivalently with CD2, CD6, and the T cell receptor (TCR), but the fraction of CD5 assocd. with CD6 was highly phosphorylated in kinase assays, in marked contrast with the low level of phosphorylation of CD5 assocd. with TCR or CD2. Examn. of protein kinases assocg. with these antigens showed that paradoxically, CD2 copptd. the highest amt. of Lck and Fyn. CD6 also assocd. with Lck, Fyn, and ZAP-70, although at lower levels but addnl. copptd. the Tec family kinase Itk, which is absent from

CD2, CD5, and TCR complexes. Lck together with Itk was the best combination of kinases, effectively phosphorylating synthetic peptides corresponding to a cytoplasmic sequence of CD5. Overall, the results suggest that CD6 has an important role in the regulation of CD5 tyrosine phosphorylation, probably as a result of its unique feature of assocg. with kinases of different families.

L6 ANSWER 2 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AB CTLA-4 negatively regulates TCR signaling, although the molecular basis for this effect has yet to be elucidated. The cytoplasmic YVKM motif, while binding to phosphatidylinositol 3-kinase, SHP-2 and the AP-1/AP-2 clathrin adaptor complexes, has been reported to play no role in CTLA-4 function. In contrast, in this study, we demonstrate that, although not essential, the YVKM motif contributes to optimal CTLA-4 blockage of TCR.zeta. or combined TCR.zeta. CD28 signaling. Significantly, dependency on the YVKM motif varied with the mode of anti-receptor presentation, where soluble **antibody** ligation was more dependent on the presence of the motif than immobilized **antibody**. Previous studies have mainly relied on the use of immobilized **antibody**. Neither SHP-2 binding, alterations in TCR.**zeta**. **chain** phosphorylation, nor ZAP-70 recruitment was involved in CTLA-4 wild-type or mutant inhibition. Overall, our findings clearly implicate the YVKM motif in optimal CTLA-4 function.

L6 ANSWER 3 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AB The activation of protein tyrosine kinase(s) (PTK) is a critical event required for the development of NK cell-mediated cytotoxicity. Here we demonstrate that the adaptor protein shc undergoes tyrosine phosphorylation during the generation of **antibody**-dependent cellular cytotoxicity (ADCC) and natural killing. In addition, we report that, upon direct or **antibody**-dependent target cell interaction, shc coprecipitates with the Src homology 2 (SH2)-containing inositol phosphatase, SHIP. To gain information on the functional role of shc in NK cytotoxicity, we overexpressed wild-type or dominant negative shc constructs in the human NKL cell line. Our findings show a consistent shc-mediated down-regulation of ADCC and natural killing. Such functional effect correlates with a perturbation of the phoshoinositide (PI) metabolism by means of a shc-mediated negative regulation of inositol 1, 4, 5 triphosphate (IP3) generation and intracellular calcium flux upon CD16 ligation. Furthermore, our data show that dominant-negative shc-mediated perturbation of shc/SHIP interaction leads to inhibition of ligand-dependent SHIP recruitment to CD16 .**zeta**. **chain** . We suggest that shc plays a role of negative adaptor by modulating SHIP recruitment to activation receptors involved in the generation of NK cytotoxic function.

L6 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2003 ACS

AB The present invention relates to a nucleic acid mol. comprising a nucleic acid sequence encoding at least one complementary detg. region (CDR) of a variable region of an **antibody**, said **antibody** specifically interacting with the extracellular domain of the human **zeta-chain**, said **antibody** being obtainable by immunizing a **rat** with Jurkat cells and subsequently with a conjugate comprising a carrier mol. and a peptide comprising the 11 N-terminal amino acids of the **rat zeta-chain** . Preferably, the (poly)peptide encoded by the nucleic acid mol. of the invention is a monospecific or bispecific **antibody**. The invention also relates to pharmaceutical compns. comprising i.a. the nucleic acid mol. or **antibody** of the invention as well as to kits comprising the aforementioned compds. Finally, the invention relates to a method for the detn. of **zeta-chain** or eta-chain expression on NK-cells, T-cells or precursors thereof employing the **antibody** of the invention. The **antibodies** are useful

for treatment and prevention of autoimmune diseases, immune deficiency, T cell malignancies, infectious diseases, and for suppression of immune response to avoid graft rejection after organ transplant.

L6 ANSWER 5 OF 25 MEDLINE

AB Immunoglobulin T-cell receptors (IgTCRs) combine the specificity of **antibodies** with the potency of cellular killing by grafting **antibody** recognition domains onto TCR signaling chains. IgTCR-modified T cells are thus redirected to kill tumor cells based on their expression of intact antigen on cell surfaces, bypassing the normal mechanism of activation through TCR-peptide-major histocompatibility complex (MHC) recognition. Melanoma is one of the most immunoresponsive of human cancers and has served as a prototype for the development of a number of immunotherapies. The target antigen for this study is the ganglioside GD3, which is highly expressed on metastatic melanoma with only minor immunologic cross-reaction with normal tissues. To determine an optimal configuration for therapy, four combinations of IgTCRs were prepared and studied: sFv-epsilon, sFv-zeta, Fab-epsilon, Fab-zeta. These were expressed on the surface of human T cells by retroviral transduction. IgTCR successfully redirected T-cell effectors in an MHC-unrestricted manner, in this case against a non-T-dependent antigen, with specific binding, activation, and cytotoxicity against GD3+ melanoma cells. Soluble GD3 in concentrations up to 100 microg/ml did not interfere with recognition and binding of membrane-bound antigen. Based on the outcomes of these structural and functional tests, the sFv-zeta construct was selected for clinical development. These results demonstrate key features that emphasize the potential of anti-GD3 IgTCR-modified autologous T cells for melanoma therapies.

L6 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2003 ACS

AB ZAP-70 is another member of Syk family tyrosine kinases which plays an essential role in growth, differentiation, and function of T lymphocytes. In this study, we report the specific expression of a 66 kDa tyrosine kinase that is specifically cross-reacted with anti-ZAP-70 **antibodies** in the developing neurons. By immunoblot and immunopptn. assay using various anti-ZAP-70 **antibodies**, a 66 kDa tyrosine kinase was detected in lysates from **rat** brain. During the development of **rat** brain, expression levels of this 66 kDa tyrosine kinase were highest around 3 wk after birth and decreased thereafter in the adult. In addn., immunoblot anal. demonstrated that this 66 kDa tyrosine kinase was expressed almost solely in the nervous system. These results suggest that this ZAP-70-related tyrosine kinase may play an important role in growth and differentiation in the developing neurons. Our observations will provide the clue to approach the regulatory system common to neurogenesis and immune response.

L6 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS

AB Adoptive transfer of tumor cell-destroying cytotoxic T-lymphocytes which express on their surface .gtoreq.1 variant epitope encoded by the CD44 gene is a useful strategy in therapy of metastasizing tumors. The lymphocytes express a fusion protein which comprises (a) a portion having a specific affinity for an amino acid sequence encoded by a variant exon of the CD44 gene [e.g. a variable domain of an **antibody** to a variant CD44 (CD44v)] and (b) a subunit of the T-cell receptor complex or of an Ig receptor or portion thereof. Nucleic acids encoding such fusion proteins are used to transform the T-lymphocytes to expression of the fusion protein. Thus, cDNA fragments encoding the VH and V.kappa. domains of monoclonal **antibody** 1.1ASML (specific for an epitope expressed by variant exon v6 of the **rat** CD44 gene) were joined by a linker sequence, coupled at the 3' end to a truncated mouse .kappa.-chain cDNA, and expressed in a mouse permanent cytotoxic T-cell line. The fusion protein was integrated into the cell membrane through the transmembrane region of the TCR .**zeta**.-**chain**

signal peptide attached at the 5' end. I.v. injection of these cells into athymic nude mice bearing BSp73AS14 **rat** tumors suppressed growth of the tumors; this effect was enhanced by simultaneous i.p. administration of recombinant human IL-2.

L6 ANSWER 8 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AB Variant proteins of the CD44 surface glycoprotein family are expressed on many different human tumors and their lymph node metastases. An epitope encoded by sequences of variant exons CD44v7 and v8 and recognized by the monoclonal **antibody** VFF17 is frequently detected in cervical cancer, whereas the normal cervical epithelium lacks expression of this epitope. We have developed an immunotherapeutic approach for cervical cancer based on the expression of this CD44v7/8 epitope. The single chain antigen-binding fragment of VFF17 was fused to a signal transducing protein (.**zeta**.-**chain**) of the T-cell receptor complex (TCR) and was introduced into a retroviral gene transfer vector. Gene transfer was applied to the murine cytotoxic T-cell line c196. All recombinant clones expressed the fusion protein on their cell surface. Functionality of the recombinant fusion protein was tested by subjection of several recombinant clones to in vitro cytotoxicity assays. CD44v7/8-expressing target cells were killed efficiently by reprogrammed c196 in an MHC-independent fashion, whereas CD44v7/8-negative cells were not affected. These transfected T cell lines will now be tested in vivo using immune-deficient mice bearing CD44v7/8-expressing tumors.

L6 ANSWER 9 OF 25 MEDLINE DUPLICATE 1
AB We are developing strategies to use naive T lymphocytes in cancer therapy. For this purpose, we are deriving T cells with specificity of recognition for defined tumor cells. To direct effector lymphocytes toward tumor cells, we have manipulated the recognition specificity of naive **rat** and mouse T lymphocytes and a mouse T-cell line. The cells were stably transduced with a chimeric T-cell receptor (TCR) component. The **zeta chain** of the TCR consists of a single transmembrane protein with a short extracellular domain and an intracellular domain for TCR signaling. We provided an extracellular tumor cell recognition domain to the **zeta chain**. Human heregulin beta1 (ligand to the erbB-3 and erbB-4 receptors) and three different single-chain **antibodies** specific for the human and **rat** Neu/erbB-2 receptors were used. One single-chain **antibody** (C11) is directed against the **rat** Neu protein, and one single-chain **antibody** (FRP5) is directed against the human erbB-2 receptor. The single-chain **antibody** (R-AK) directed against the Mr 14,000 fusion protein of orthopox viruses served as a control. An efficient procedure was devised to introduce the chimeric genes into primary **rat** and mouse T lymphocytes. Retrovirus-producing packaging cell lines were cocultured with the T cells activated by phytohemagglutinin and interleukin 2. T-cell lines were transduced by exposure to retrovirus-containing supernatants from helper cell lines. Expression of the fusion genes was determined by fluorescence-activated cell sorting analysis. More than 80% of the naive **rat** and mouse T cells and 85-100% of the cells from the established T-cell lines expressed the fusion genes within 48 h after infection. The expression of the fusion genes was maintained for at least 10 days after infection. Target cells expressing Neu/erbB-2, erbB-3, or erbB-4 were lysed in vitro with high specificity by T cells expressing the corresponding recognition proteins. No selection of a marker gene is necessary to confer a predetermined recognition specificity. The described experiments are important for a gene therapy approach to cancer treatment with autologous T cells.

L6 ANSWER 10 OF 25 MEDLINE DUPLICATE 2
AB Variants of the CD44 protein family containing sequences encoded by variant exon 6 (v6) are involved in the metastatic spread of **rat**

and human tumors. The **rat**-specific **antibody** 1.1ASML, which recognizes a v6 epitope, interferes with metastatic dissemination of a **rat** pancreatic carcinoma. The single-chain antigen-binding fragment of this monoclonal **antibody** was fused to the **zeta-chain** of the T-cell receptor complex. The appropriate fusion gene was incorporated into a retroviral gene transfer vector. Murine cytotoxic T lymphocytes (CTLs) were infected, and cellular clones which express the single-chain **zeta-chain** fusion protein on their cell surface were selected. These CTLs are not MHC-restricted in their CD44v6 recognition and exhibit in vitro lytic activity toward cells expressing CD44 variants comprising exon v6. Tumor cell xenografts grown in athymic nude mice are suppressed in their growth upon infusion of the genetically manipulated CTLs. Our data indicate that the CD44v6 epitope is an effective target for immune tumor therapy and demonstrate the efficacy of genetically engineered CTLs in targeting tumors expressing such epitopes.

L6 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

AB CD3-epsilon and the **zeta-chain** of the bovine T-cell receptor (TCR) are two invariant molecules with an important role in signal transduction via the TCR/CD3 complex. The nucleotide sequence of a bovine CD3-epsilon cDNA clone containing the complete coding sequence was determined and the deduced amino acid (aa) sequence compared to that of other species. The cytoplasmic domains of the different CD3-epsilon clearly show a higher degree of conservation than the extracellular domains. Bovine CD3-epsilon produced in Escherichia coli using different bacterial expression vectors was recognised by **antibodies** (Ab) directed against the intracytoplasmic domain of human CD3-epsilon. A partial bovine TCR-**zeta-chain** cDNA was generated by the polymerase chain reaction (PCR) using primers that were based on sequences that are conserved between different species; 3' and 5' RACE-PCR were carried out to obtain the complete TCR-**zeta-chain** cDNA sequence. A comparison of the predicted TCR-**zeta-chain** aa sequence reveals that the GDP/GTP-binding motif, which is conserved in other species, shows marked differences in the bovine and ovine TCR-**zeta-chains**. In contrast to CD3-epsilon, the short also shows a high degree of identity. Ab were raised against the TCR-**zeta-chain**, produced as a glutathione S-transferase fusion protein in E. coli, and were used in Western blot analysis to further characterize TCR-**zeta-chain** expression in T-cells. These reagents provide valuable tools for the study of signal transduction pathways in normal and transformed bovine T-cells.

L6 ANSWER 12 OF 25 MEDLINE

L6 ANSWER 13 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB A cDNA encoding a signal transduction protein with a Src homology 2 (SH2) domain and a tyrosine phosphorylation site mas cloned from a **rat** lymph node cDNA library, This protein, which we designate Lnk, has a calculated molecular weight of 33,988. When T lymphocytes were activated by **antibody**-mediated crosslinking of the T-cell receptor and CD4, Lnk became tyrosine phosphorylated, In activated T lymphocytes, phospholipase C gamma(1), phosphatidylinositol 3-kinase, and Grb-2 coimmunoprecipitated with Lnk. Our results suggest that Lnk becomes tyrosine phosphorylated and links the immediate tyrosine phosphorylation signals of the TCR to the distal phosphatidylinositol 3-kinase, phospholipase C gamma(1) and Ras signaling pathways through its multifunctional tyrosine phosphorylation site.

L6 ANSWER 14 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB In mast cells, antigen-mediated aggregation of the high-affinity receptor for immunoglobulin E, Pc epsilon RI, stimulates tyrosine phosphorylation and activation of multiple signaling pathways leading to

the release of several classes of mediators of the allergic response. Early events induced upon cross-linking of Fc epsilon RI include tyrosine phosphorylation of Fc epsilon RI subunits and activation of the tyrosine kinase p72(syk) (Syk), Which binds to tyrosine-phosphorylated Fc epsilon RI, Clustering of Syk, as a result of its interaction with aggregated Fc epsilon RI, may play a role in activating one or more of the signaling pathways leading to mediator release, To test this possibility, Syk was introduced into a model mast cell line (**rat** basophilic leukemia cells) as part of a chimeric transmembrane protein containing the extracellular and transmembrane domains of CD16 and CD7, respectively, Clustering of the Syk chimera, using **antibodies** against CD16, was found to be sufficient to stimulate early and late events normally induced by clustering of Fc epsilon RI, Specifically, aggregation of Syk induced degranulation, leukotriene synthesis, and expression of cytokine genes, Induction of mediator release was dependent on the kinase activity of Syk Consistent with this finding, clustering of Syk also induced the tyrosine phosphorylation of a profile of proteins, including phospholipase C-gamma 1 and mitogen-activated protein kinase, similar to that induced upon clustering of Fc epsilon RI, These results strongly suggest that Syk is an early and critical mediator of multiple signaling pathways that emanate from the Fc epsilon RI receptor and give rise to the allergic response.

L6 ANSWER 15 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AB We studied the coupling of the TCR/CD3 complex to a T cell effector function, namely Fas-based T cell-mediated cytotoxicity. Encounter or re-encounter with antigen was mimicked by treating 5 d mixed lymphocyte culture cells or T cell hybridomas with anti-CD3 **antibody**. This TCR/CD3 engagement induced swift expression of Fas-based cytotoxicity in these cells. Induction of Fas-based cytotoxicity was Ca2+-dependent, while its execution was not; induction was sensitive to macromolecular synthesis inhibitors, in line with a demonstrable increase of the Fas ligand (Fas-L) message. We also used T cell hybridomas transfected with various constructs to dissect the involvement of distinct components of the TCR/CD3 complex. The cytoplasmic domain of the CD3 .**zeta**. **chain** was able to transduce by itself a signal leading to Fas-L expression, unless there were mutations in its activation receptor homology sequence 1 (ARH-1) motifs. On the one hand, these findings are relevant to signal transduction pathways coupled to the TCR/CD3, and on the other hand, to the involvement of Fas-based T cell-mediated cytotoxicity in various physiological and possibly pathophysiological situations.

L6 ANSWER 16 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB Crosslinking of the B-cell receptor (BCR) for antigen to low-affinity receptors for IgG (Fc gamma RII) inhibits B-cell activation induced by BCR aggregation. The cell-triggering properties of the BCR depend on tyrosine-containing activation motifs (TAM), in the intracytoplasmic domain of its Ig alpha and Ig beta subunits. TAMs also account for the cell-triggering capabilities of the T-cell receptor (TCR) for antigen, in T lymphocytes, and of the high-affinity receptor for IgE (Fc epsilon RI), in mast cells. Using as a model, **rat** basophilic leukemia cells (RBL-2H3) stably transfected with cDNA encoding wild-type or mutated murine or human Fc gamma RIIB and chimeric molecules having the intracytoplasmic domain of the FcR gamma subunit or of TCR-CD3 zeta subunit, we found that the inhibitory properties of Fc gamma RII are neither restricted to B cells nor to BCR-dependent cell activation, but can be extended to other cells and, as a general rule, to TAM-dependent cell activation.

L6 ANSWER 17 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB Aggregation of the high affinity IgE receptors (Fc epsilon RI) on **rat** basophilic leukemia RBL-2H3 cells results in protein tyrosine

phosphorylations. Previously we reported that there is prominent tyrosine phosphorylation of similar to 72-kDa proteins (pp72) and that the tyrosine kinase p72(syk) is one component of pp72. Here we studied further the relationship of p72(syk) to pp72. The aggregation of Fc epsilon RI induced the activation of p72(syk) which was parallel to its tyrosine phosphorylation. By in vitro kinase assay of immune complexes purified with anti-phosphotyrosine **antibodies**, p72(syk) was the major pp72 tyrosine kinase. However, by immunoblotting with anti-phosphotyrosine **antibodies**, p72(syk) was a minor component of pp72. The heterogeneous nature of pp72 was indicated by different studies. Under optimum conditions of one-dimensional sodium dodecyl sulfate-polyacrylamide gel electrophoresis, pp72 consisted of a heterogeneous group of 69-, 71-, and 72-kDa tyrosine-phosphorylated proteins. There were differences in the tyrosine phosphorylation of these proteins in cells activated in the absence of extracellular calcium or when stimulation was with the calcium ionophore A23187 or with phorbol myristate acetate. One of the proteins migrating at 69 kDa was p72(syk). By two-dimensional gel electrophoresis pp72 was found to consist of multiple tyrosine-phosphorylated proteins including 71-80-kDa proteins that associate with p53/56(lyn). A 75-kDa tyrosine-phosphorylated protein, different from pp72, was identified as p75(HS1) (SPY75). These results demonstrate the heterogeneous nature of the pp72 and that p72(syk) is activated after Fc epsilon RI aggregation.

L6 ANSWER 18 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB Protein-tyrosine phosphorylation plays a critical role in the high-affinity IgE receptor (FcepsilonRI) signaling. Here we investigated the involvement of the tyrosine kinase p72syk in FcepsilonRI signaling in the **rat** mast cell line RBL-2H3. Specific **antibodies** were raised against peptides synthesized on the basis of the deduced peptide sequence of an essentially full-length **rat** syk cDNA. The expression of p72syk in RBL-2H3 cells was demonstrated with these **antibodies**. The aggregation of FcepsilonRI led to the tyrosine phosphorylation of p72syk that was detected after 15 s of stimulation, reached a plateau by 5 min, and was not induced by calcium influx or protein kinase C activation. Association of p72syk with the tyrosine phosphorylated FcepsilonRIgamma chain was detected only after receptor aggregation. We previously demonstrated that aggregation of the FcepsilonRI on mast cells results in the tyrosine phosphorylation of a 72-kDa protein (pp72) involved in IgE signaling. The depletion of p72syk from RBL-2H3 cell lysates resulted in only a slight decrease in the amount of pp72. These results demonstrate that pp72 is composed of several phosphoproteins and identify p72syk as one component of pp72. These data, together with recent observations in T cells, indicate that the interaction between p72syk-related tyrosine kinases and zeta-related proteins could play an important role in signal transduction.

L6 ANSWER 19 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.DUPLICATE 3

AB Study of the T-cell repertoire in humans has been hampered by the lack of monoclonal **antibodies** (mAbs) to the T-cell receptor (TCR) variable region (V) gene products. We describe a method for producing mAbs to the human TCR .beta.- chain V (V(.beta.)) gene products in which mice were immunized with a **rat** basophil cell line (RBL-2H3) transfected with the extracellular domain of the TCR heterodimer fused to the .**zeta**. **chain** of CD3. These cells acted as excellent immunogens for raising anti-TCR mAb and also formed the basis of a rapid screening assay. We generated mAbs against V(.beta.) protein of the TCR, showed that these mAbs stained .simeq.1% of peripheral blood T cells, and further showed that the mAbs could stimulate proliferation of these T cells. We then characterized the mAbs by amplifying TCR cDNA derived from mAb-stimulated cells and sequencing the .beta. chain. All clones sequenced used the V(.beta.)7.1 chain, proving conclusively that the mAbs generated were specific for V(.beta.)7.1 subfamily. This method

generates mAbs to human TCR V(.beta.) proteins efficiently and might allow production of a complete panel of mAbs directed against human TCR V(.beta.) proteins.

L6 ANSWER 20 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB Several new **rat** class III FcgammaR isoforms are described here, extending the genetic complexity of this receptor family and further distinguishing **rat** CD1 6 from mouse CD16, represented by only one receptor isoform, and human CD16, represented by only two isoforms. RNase protection assays reveal that three **rat** tumor cell lines-RBL-1 basophilic leukemia cells, RM-SV1 macrophages, and CRNK-16 NK cells-all coordinately express multiple and probably identical rtFcgammaRIII-related transcripts in similar relative proportions but at significantly different levels. These results indicate that no single isoform predominates in these cell types but that the overall level of rtFcgammaRIII-related transcripts is differentially regulated. Two of the rtFcgammaRIII isoforms found to have extensive amino acid sequence differences in their second extracellular (EC2) domains are shown to bind **rat** and mouse IgG subclasses differently. This result suggests that the receptor isoform diversity in this species may function as a mechanism for extending the IgG-binding capacity of **rat** leukocytes. Cloned cDNA for the **rat** CD3zeta protein was also isolated in this study and its ability to augment surface expression of class III FcgammaR was tested by rosetting of cDNA-transfected COS cells. Like the structurally homologous mouse CD3zeta, **rat** CD3zeta fails to promote surface expression of FcgammaRIII, sharply contrasting the efficient receptor expression produced by human CD3zeta. Variations in the transmembrane amino acid sequences correlate with the divergent capacities of these CD3zeta molecules to augment receptor expression. The high levels of CD3zeta message expressed in **rat** NK cells may indicate that other unidentified heterosubunits are required for assembly of **rat** CD3zeta into functional CD16 receptors.

L6 ANSWER 21 OF 25 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

AB The coreceptor hypothesis postulates that physical association of CD4 with the TCR is required for effective signaling for T cell activation. A variety of studies has suggested that the coreceptor function of CD4 allows responses to 10- to 100-fold lower levels of peptide:self MHC class II ligand. We test the hypothesis of CD4 physical association with the TCR in two different ways. First, we use a panel of soluble **antibodies** directed at different TCR epitopes to activate a cloned T cell line, and show that activation by **antibodies** directed at a particular TCR epitope can be inhibited by anti-CD4 **antibodies** binding to a certain CD4 epitope. These effects establish that the interaction of CD4 and the TCR occurs in a specific orientation. Second, we use the same system to provide evidence that the physical association of CD4 with the TCR is required for effective tyrosine phosphorylation of the TCR . **zeta**.-**chain** subunit, presumably reflecting delivery of p56(lck) (lck) to the TCR. Only anti-TCR **antibodies** that induce physical association of CD4 with the TCR as monitored by cocapping can induce efficient tyrosine- phosphorylation of the TCR .**zeta**.-**chain**, unless second **antibodies** are used to force CD4 and the TCR to associate. Furthermore, the phosphorylation of the TCR . **zeta**.-**chain** exactly parallels physical association in time and drug sensitivity. We conclude from these studies that stimuli that drive physical association of CD4 and the TCR strongly favor T cell activation, supporting the coreceptor hypothesis of CD4 function.

L6 ANSWER 22 OF 25 MEDLINE DUPLICATE 4

AB The **zeta chain** of the T-cell antigen receptor is the prototype of a family of proteins that exist as disulfide-linked dimers and are subunits of the T-cell antigen receptor and both IgE and IgG binding Fc receptors. Two related genes encode the zeta and gamma

proteins. In this study we examine the ability of chimeric proteins consisting of the extracellular domain of the alpha chain of the interleukin 2 receptor (Tac) and the cytoplasmic domain of either zeta or gamma to activate cells when expressed in either T cells or **rat** basophilic leukemia cells. The zeta and gamma chimera were effective at eliciting interleukin 2 production in T cells and serotonin release in **rat** basophilic leukemia cells when externally cross-linked. Cytoplasmic-tail deletion mutants of zeta and gamma were constructed and used to verify the specificity of cell activation by these chimeric proteins. Signaling potencies of complementary mutants having the zeta tail truncated in position 108 or deleted from positions 66 through 114 suggested the presence of several functional domains in zeta.

L6 ANSWER 23 OF 25 SCISEARCH COPYRIGHT 2003 ISI (R)

AB In the present report, we demonstrated that modulation of CD26 from T cell surface induced by anti-CD26 (1F7) led to enhanced phosphorylation of CD3 zeta-tyrosine residues and increased CD4 associated p56lck tyrosine kinase activity. We further showed that CD26 was comodulated on the T cell surface with CD45, a known membrane-linked protein tyrosine phosphatase and that anti-CD26 was capable of precipitating CD45 from T cell lysates. These findings strongly suggest that CD26 may be closely associated with the CD45 protein tyrosine phosphatase on T cell surface and further support the notion that the interaction of CD26 with CD45 results in enhanced tyrosine kinase activity, **zeta-chain** phosphorylation, and T cell activation.

L6 ANSWER 24 OF 25 MEDLINE DUPLICATE 5

AB Crosslinking of CD2 antigen on T lymphocytes and natural killer (NK) cells leads to a rise in cytoplasmic-free Ca2+ concentration ([Ca2+]i). However, CD2 seems unlikely to interact directly with the second messenger pathways since signaling via CD2 is poor in T cells that lack the T cell receptor (TCR) and is absent in L cells or insect cells that express CD2. In contrast, NK cells that are also TCR- can be triggered via CD2, but it is unclear as to whether the CD16 Fc receptor (FcR) may facilitate this effect. The CD16 transmembrane molecule is expressed in a complex with the zeta homodimer or the zeta/gamma heterodimer and these dimers are also associated with the TCR complex. Thus, it seemed that **zeta chains** may provide the link between signaling on NK cells and T cells. This could be tested on TCR- cells since when CD16 is transfected into T cells it is expressed in a complex with TCR zeta homodimer or the zeta/gamma heterodimer. At first, potentiation of CD2 signaling was seen on TCR- Jurkat cells expressing CD16, but this was found to be dependent on trace levels (1%) of IgG in F(ab')2 **antibody** preparations. With pure F(ab')2, the effect was lost. Signaling on a **rat** NK cell line was also re-examined with F(ab')2 **antibodies** that had no IgG contamination, and again no signal transduction via CD2 was seen. We thus conclude that there is no clear evidence for potent signaling via CD2 on cells that lack a TCR complex and that TCR **zeta chain** expressed at the cell surface is not sufficient to potentiate signaling via CD2 as measured by an increase in [Ca2+]i.

L6 ANSWER 25 OF 25 MEDLINE

AB The T-cell antigen receptor is a multisubunit complex consisting of at least seven chains. Based upon structural and genetic considerations, we have divided these chains into three groups. The alpha and beta subunits (Ti) are the clonotypic chains responsible for antigen recognition. Three chains that are invariant among all T-cells define the CD3 complex. These include the CD3 gamma, delta, and epsilon chains. The **zeta chain** is a distinct component that, like the CD3 chains, is invariant among all T-cells. In the majority of receptors, zeta is found as a disulfide-linked homodimer. We have recently shown that approximately 10% of zeta is disulfide-linked to a chain which we have called eta. A preliminary model has been proposed, suggesting that there are two

subclasses of receptors, depending upon the presence within the complex of either the zeta-zeta homodimer or the zeta-eta heterodimer. Evidence has been presented that these two subclasses may perform distinct signaling functions. In this paper the eta chain is characterized to determine whether it is structurally related to the **zeta chain** and, in particular, whether it might represent a post-translational modification of zeta. We can identify specific antigenic epitopes that are shared by both zeta and eta. However, not all **antibodies** raised against zeta can directly recognize eta. The apparent molecular mass of eta is 22 kDa, whereas zeta has a molecular mass of 16 kDa. We are unable to demonstrate any post-translational covalent modifications of eta to explain the difference in apparent molecular weight. These include phosphorylation, glycosylation, or sulfation. Amino acid incorporation studies demonstrate that the amino acid composition of eta is distinct from that of zeta. All of the eta in a T-cell is found in association with the rest of the components of the T-cell receptor. In addition, our anti-eta **antibodies** allow us to directly recognize human eta, which has an apparent molecular mass of approximately 23 kDa. Thus, eta and zeta appear to be related but distinct proteins, and we would propose that eta is the second member of the zeta group of components of the T-cell receptor.

```
=> s zeta chain DNA
L7            0 ZETA CHAIN DNA

=>

=> d his

     (FILE 'HOME' ENTERED AT 11:09:24 ON 25 FEB 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:09:36 ON
     25 FEB 2003
L1          4147 S ZETA CHAIN
L2          1106 S L1 AND ANTIBODY
L3             1 S L2 AND RAT ZETA CHAIN
L4           100 S L1 AND RAT
L5            39 S L4 AND ANTIBODY
L6            25 DUP REMOVE L5 (14 DUPLICATES REMOVED)
L7             0 S ZETA CHAIN DNA

=> s l1 and anti-zeta chain
L8            5 L1 AND ANTI-ZETA CHAIN

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9             1 DUP REMOVE L8 (4 DUPLICATES REMOVED)

=> d l9 cbib abs

L9   ANSWER 1 OF 1     MEDLINE                              DUPLICATE 1
96290429  Document Number: 96290429.    PubMed ID: 8704179.   T cells from
     patients with Hodgkin's disease have a defective T-cell receptor
     zeta chain expression that is reversible by T-cell
     stimulation with CD3 and CD28. Renner C; Ohnesorge S; Held G; Bauer S;
     Jung W; Pfitzenmeier J P; Pfreundschuh M. (Medical Department I,
     University of the Saarland, Homburg, Germany. ) BLOOD, (1996 Jul 1) 88 (1)
     236-41.  Journal code: 7603509. ISSN: 0006-4971. Pub. country: United
     States. Language: English.
AB   To investigate the mechanisms underlying the deficiency of T lymphocytes
     from patients with Hodgkin's disease, we investigated the expression of
     the T-cell receptor (TCR) zeta chain in patients with
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Hodgkin's disease. By flow cytometry using an **anti-zeta chain** monoclonal antibody, peripheral blood T lymphocytes from patients with untreated Hodgkin's disease were shown to express decreased levels of the TCR **zeta chain**. After stimulation by combined CD3 and CD28 cross-linking, T cells from Hodgkin's disease patients upregulated **zeta chain** protein expression to normal values within 48 hours and achieved a cytolytic potential and levels of interleukin (IL)-2 secretion that were not different from T cells obtained from healthy controls. These results show that downregulation of the TCR **zeta chain** in Hodgkin's T lymphocytes is a reversible event. Costimulation of CD3 and CD28 is a novel approach for overcoming the T-cell deficiency in Hodgkin's disease and might be exploited clinically. As upregulation of the **zeta chain** can also be achieved using bispecific monoclonal antibodies (BI-MoAbs) with specificity for tumor antigens and CD3 and CD28, respectively, an immunotherapy with CD3/CD30 and CD28/CD30 Bi-MoAbs may overcome and should therefore, not be jeopardized by the inherent T-cell deficiency in patients with Hodgkin's disease.

=> s l2 and rat zeta chain
L10 1 L2 AND RAT ZETA CHAIN

=> d l10 cbib abs

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
2000:53887 Document No. 132:106967 Immunological reagent specifically interacting with the extracellular domain of the human **zeta chain**. Reiter, Christian (Connex G.m.b.H., Germany). PCT Int. Appl. WO 2000003016 A1 20000120, 79 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP4838 19990709. PRIORITY: EP 1998-112867 19980710.

AB The present invention relates to a nucleic acid mol. comprising a nucleic acid sequence encoding at least one complementary detg. region (CDR) of a variable region of an **antibody**, said **antibody** specifically interacting with the extracellular domain of the human **zeta-chain**, said **antibody** being obtainable by immunizing a rat with Jurkat cells and subsequently with a conjugate comprising a carrier mol. and a peptide comprising the 11 N-terminal amino acids of the **rat zeta-chain**. Preferably, the (poly)peptide encoded by the nucleic acid mol. of the invention is a monospecific or bispecific **antibody**. The invention also relates to pharmaceutical compns. comprising i.a. the nucleic acid mol. or **antibody** of the invention as well as to kits comprising the aforementioned compds. Finally, the invention relates to a method for the detn. of **zeta-chain** or eta-chain expression on NK-cells, T-cells or precursors thereof employing the **antibody** of the invention. The **antibodies** are useful for treatment and prevention of autoimmune diseases, immune deficiency, T cell malignancies, infectious diseases, and for suppression of immune response to avoid graft rejection after organ transplant.

=> s l2 and human zeta chain
L11 2 L2 AND HUMAN ZETA CHAIN

=> dup remove l11

PROCESSING COMPLETED FOR L11
L12 2 DUP REMOVE L11 (0 DUPLICATES REMOVED)

=> d l12 1-2 cbib abs

L12 ANSWER 1 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2002:129949 Document No.: PREV200200129949. Co-expression of a CD19-specific immunoreceptor and CD28 in primary T-cells provides co-stimulation and augments efficacy in ALL and NHL. Topp, Max S. (1); Riddell, Stanley R. (1); Greenberg, Philip D. (1); Forman, Stephen J.; Raubitschek, Andrew; Jensen, Michael C.. (1) Immunology, Fred Hutchinson Cancer Research Center, Seattle, WA USA. Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 122a. http://www.bloodjournal.org/. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001 ISSN: 0006-4971. Language: English.
AB Acute lymphoblastic leukemia (ALL) and high-grade Non-Hodgkin lymphomas (NHL) frequently recur following conventional chemotherapy or autologous/allogeneic stem cell transplant. Adoptive transfer of antigen-specific T-cell represents an actractive therapeutic modality for targeting minimal residual disease without the toxicity related to donor lymphocyte infusion. We took advantage of the tissue specific expression of CD19 during B-cell ontogeny and the availability of high-affinity **antibodies** to design a chimeric immunoreceptor consisting of the variable light and heavy regions of a CD19-specific monoclonal **antibody** fused to the human IgG4 Fc, the transmembrane region of human CD4 and as signaling domain the cytoplasmic portion of the **human zeta-chain**. A DNA construct encoding the chimeric immunoreceptor was introduced into primary human T-cells by plasmid transfection and chimeric immonoreceptor expressing CD4+ or CD8+ T-cell clones were selected by limiting dilution and screening for cytotoxicity against CD19+ targets. Clones with documented expression levels of the chimeric immunoreceptor in CD4+ and CD8+ T-cell clones demonstrated redirected specific lysis of CD19+ ALL and NHL cells. Strikingly, all cytolytic CD19-specific CD4+ and CD8+ T-cell clones were negative for the expression of CD28, a co-stimulatory molecule expressed in all naive T-cells but lost in 25-50% of CD8+ T-cells and a minor fraction of CD4+ memory T-cells. Engagement of CD28 cooperates with T-cell receptor signaling to enhance cytokine production, stabilize cytokine mRNA and induction of the antiapoptotic protein BcL XL. The ligands for CD28, CD80 and CD86, are expressed at low levels by the majority of ALL and B-NHL cells. However, this low level of CD80 and CD86 expression can costimulate primary T-cells suggesting that expression of CD28 on T-cells may facilitate an effective antitumor response. Thus, CD28 was expressed into CD19-specific CD28-/CD4+ and CD8+ T-cell clones. The cytolytic potency of CD28+ CD19-specific CD4+ and CD8+ T-cell clones was maintained as measured by a 4-hr chromium release assay. In addition, target recognition by CD19 specific CD4+ and CD8+ T-cell clones engineered to express CD28 triggered production of IL-2 and resulted in robust autocrine proliferation. Conversely, no IL-2 production and autocrine proliferation was detected in the parental CD28- CD19-specific CD4+ and CD8+ T-cell clones. Preliminary results in treating NHL/Daudi-bearing NOD/SCID mice with adoptively transferred CD19-specific T-cells modified to express CD28 displayed augmented anti-tumor potency. Thus, the combined introduction of a CD19-specific chimeric immunoreceptor and CD28 into human CD4+ and CD8+ T-cells may augment the anti-tumor potency of adoptively transferred CD19-specific CD4+ and CD8+ T-cell clones in vivo.

L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
2000:53887 Document No. 132:106967 Immunological reagent specifically interacting with the extracellular domain of the **human zeta chain**. Reiter, Christian (Connex G.m.b.H., Germany). PCT Int. Appl. WO 2000003016 A1 20000120, 79 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU,

CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2.
APPLICATION: WO 1999-EP4838 19990709. PRIORITY: EP 1998-112867 19980710.

AB The present invention relates to a nucleic acid mol. comprising a nucleic acid sequence encoding at least one complementary detg. region (CDR) of a variable region of an **antibody**, said **antibody** specifically interacting with the extracellular domain of the **human zeta-chain**, said **antibody** being obtainable by immunizing a rat with Jurkat cells and subsequently with a conjugate comprising a carrier mol. and a peptide comprising the 11 N-terminal amino acids of the rat **zeta-chain**. Preferably, the (poly)peptide encoded by the nucleic acid mol. of the invention is a monospecific or bispecific **antibody**. The invention also relates to pharmaceutical compns. comprising i.a. the nucleic acid mol. or **antibody** of the invention as well as to kits comprising the aforementioned compds. Finally, the invention relates to a method for the detn. of **zeta-chain** or eta-chain expression on NK-cells, T-cells or precursors thereof employing the **antibody** of the invention. The **antibodies** are useful for treatment and prevention of autoimmune diseases, immune deficiency, T cell malignancies, infectious diseases, and for suppression of immune response to avoid graft rejection after organ transplant.

```
=> s l2 and mouse zeta-chain
L13           0 L2 AND MOUSE ZETA-CHAIN

=> s l2 and mouse zeta chain
L14           0 L2 AND MOUSE ZETA CHAIN

=> s mouse zeta chain
L15           0 MOUSE ZETA CHAIN

=> d his

     (FILE 'HOME' ENTERED AT 11:09:24 ON 25 FEB 2003)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:09:36 ON
     25 FEB 2003
L1          4147 S ZETA CHAIN
L2          1106 S L1 AND ANTIBODY
L3             1 S L2 AND RAT ZETA CHAIN
L4           100 S L1 AND RAT
L5            39 S L4 AND ANTIBODY
L6            25 DUP REMOVE L5 (14 DUPLICATES REMOVED)
L7             0 S ZETA CHAIN DNA
L8             5 S L1 AND ANTI-ZETA CHAIN
L9             1 DUP REMOVE L8 (4 DUPLICATES REMOVED)
L10            1 S L2 AND RAT ZETA CHAIN
L11            2 S L2 AND HUMAN ZETA CHAIN
L12            2 DUP REMOVE L11 (0 DUPLICATES REMOVED)
L13            0 S L2 AND MOUSE ZETA-CHAIN
L14            0 S L2 AND MOUSE ZETA CHAIN
L15            0 S MOUSE ZETA CHAIN

=> s l1 and mouse
L16        1190 L1 AND MOUSE

=> s l16 and anti-zeta chain
```

L17 0 L16 AND ANTI-ZETA CHAIN

=> s (Reiter c?/au)
L18 622 (REITER C?/AU)

=> s l18 and zeta chain
L19 1 L18 AND ZETA CHAIN

=> d l19 cbib abs

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
2000:53887 Document No. 132:106967 Immunological reagent specifically interacting with the extracellular domain of the human **zeta chain**. **Reiter, Christian** (Connex G.m.b.H., Germany).
PCT Int. Appl. WO 2000003016 A1 20000120, 79 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP4838 19990709. PRIORITY: EP 1998-112867 19980710.
AB The present invention relates to a nucleic acid mol. comprising a nucleic acid sequence encoding at least one complementary detg. region (CDR) of a variable region of an antibody, said antibody specifically interacting with the extracellular domain of the human **zeta-chain**, said antibody being obtainable by immunizing a rat with Jurkat cells and subsequently with a conjugate comprising a carrier mol. and a peptide comprising the 11 N-terminal amino acids of the rat **zeta-chain**. Preferably, the (poly)peptide encoded by the nucleic acid mol. of the invention is a monospecific or bispecific antibody. The invention also relates to pharmaceutical compns. comprising i.a. the nucleic acid mol. or antibody of the invention as well as to kits comprising the aforementioned compds. Finally, the invention relates to a method for the detn. of **zeta-chain** or eta-chain expression on NK-cells, T-cells or precursors thereof employing the antibody of the invention. The antibodies are useful for treatment and prevention of autoimmune diseases, immune deficiency, T cell malignancies, infectious diseases, and for suppression of immune response to avoid graft rejection after organ transplant.

=> s l18 and antibody
L20 155 L18 AND ANTIBODY

=> dup remove l20
PROCESSING COMPLETED FOR L20
L21 68 DUP REMOVE L20 (87 DUPLICATES REMOVED)

=> s l21 and zeta
L22 1 L21 AND ZETA

=> d l21 1-68 cbib

L21 ANSWER 1 OF 68 CAPLUS COPYRIGHT 2003 ACS
2001:284211 Document No. 134:307603 A rapid immunochromatographic assay for cell surface markers to detect acid-resistant microorganisms in the stool. **Reiter, Christian**; Cullmann, Gerhard; Lakner, Meret; Truee, Andreas; Dehnert, Sonja; Schwartz, George (Connex Gesellschaft zur Optimierung von Forschung und Entwicklung m.b.H., Germany). PCT Int. Appl. WO 2001027612 A2 20010419, 90 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE,

DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (German). CODEN: PIXXD2. APPLICATION: WO 2000-EP10057 20001012. PRIORITY: EP 1999-120351 19991012; EP 2000-105592 20000316; EP 2000-107028 20000331; EP 2000-110110 20000510.

L21 ANSWER 2 OF 68 CAPLUS COPYRIGHT 2003 ACS
2000:842260 Document No. 134:13992 Albumin/spermidine/**antibody** mixture for neutralizing inhibitors of nucleic acid-modifying enzymes. **Reiter, Christian** (Connex Gesellschaft zur Optimierung von Forschung und Entwicklung m.b.H., Germany). PCT Int. Appl. WO 2000071698 A2 20001130, 42 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (German). CODEN: PIXXD2. APPLICATION: WO 2000-EP3933 20000502. PRIORITY: DE 1999-19919942 19990430.

L21 ANSWER 3 OF 68 CAPLUS COPYRIGHT 2003 ACS
2000:314924 Document No. 132:331679 Detection of Helicobacter pylori and other acid-resistant microorganisms in stool using immunoassays. **Reiter, Christian**; Cullmann, Gerhard; Friedrichs, Ulrike; Heppner, Petra; Lakner, Meret; Ringeis, Achim (Connex G.m.b.H., Germany). PCT Int. Appl. WO 2000026671 A1 20000511, 84 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (German). CODEN: PIXXD2. APPLICATION: WO 1999-EP8212 19991029. PRIORITY: EP 1998-120517 19981029; EP 1998-120687 19981106.

L21 ANSWER 4 OF 68 CAPLUS COPYRIGHT 2003 ACS
2000:84858 Document No. 132:150605 Anti-hepatitis c virus **antibody** and uses thereof. **Reiter, Christian**; Habersetzer, Francois; Fournillier, Anne; Trepo, Christian; Desgranges, Claude; Inchauspe, Genevieve (Connex Gesellschaft Zur Optimierung Von Forschung Und Entwicklung Mbh, Germany; Institut National De La Sante Et De La Recherche Medicale (I.N.S.E.R.M.)). PCT Int. Appl. WO 2000005266 A1 20000203, 64 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP5173 19990720. PRIORITY: EP 1998-113595 19980721.

L21 ANSWER 5 OF 68 CAPLUS COPYRIGHT 2003 ACS
2000:53887 Document No. 132:106967 Immunological reagent specifically interacting with the extracellular domain of the human zeta chain. **Reiter, Christian** (Connex G.m.b.H., Germany). PCT Int. Appl. WO 2000003016 A1 20000120, 79 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU,

AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-EP4838 19990709. PRIORITY: EP 1998-112867 19980710.

L21 ANSWER 6 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
2001:210576 Document No.: PREV200100210576. A human monoclonal **antibody** recognizing different HCV genotypes suggesting convincing therapeutic potential. Barner, M. (1); Pueschke, S. (1); Ulferts, F. (1); Raum, T. (1); Inchauspe, G.; Dubuisson, J.; Diepolder, H. M.; **Reiter, C. (1)**; Mueller, H. M. (1). (1) Connex GmbH, Martinsried Germany. Immunobiology, (November, 2000) Vol. 203, No. 1-2, pp. 343-344. print. Meeting Info.: Joint Annual Meeting of the German and Dutch Societies of Immunology Duseldorf, Germany November 29-December 02, 2000 ISSN: 0171-2985. Language: English. Summary Language: English.

L21 ANSWER 7 OF 68 SCISEARCH COPYRIGHT 2003 ISI (R)
1999:791091 The Genuine Article (R) Number: 244XA. Detection of humoral rejection in human cardiac allografts by assessing the capillary deposition of complement fragment C4d in endomyocardial biopsies. Behr T M (Reprint); Feucht H E; Richter K; **Reiter C**; Spes C H; Pongratz D; Uberfuhr P; Meiser B; Theisen K; Angermann C E. SMITHKLINE BEECHAM PHARMACEUT, DEPT CARDIOVASC PHARMACOL, 709 SWEELAND RD, POB 1539, UW 2510, KING OF PRUSSIA, PA 19406 (Reprint); UNIV MUNICH, KLINIKUM GROSSHADERN, DEPT CARDIOL, D-8000 MUNICH, GERMANY. JOURNAL OF HEART AND LUNG TRANSPLANTATION (SEP 1999) Vol. 18, No. 9, pp. 904-912. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 . ISSN: 1053-2498. Pub. country: USA; GERMANY. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

L21 ANSWER 8 OF 68 MEDLINE DUPLICATE 1
1999196580 Document Number: 99196580. PubMed ID: 10098944. Three-dimensional reconstruction of the antennal lobe in Drosophila melanogaster. Laissue P P; **Reiter C**; Hiesinger P R; Halter S; Fischbach K F; Stocker R F. (Institute of Zoology and Program in Neuroscience, University of Fribourg, Switzerland.) JOURNAL OF COMPARATIVE NEUROLOGY, (1999 Mar 22) 405 (4) 543-52. Journal code: 0406041. ISSN: 0021-9967. Pub. country: United States. Language: English.

L21 ANSWER 9 OF 68 MEDLINE DUPLICATE 2
1999177089 Document Number: 99177089. PubMed ID: 10077484. A novel superoxide dismutase-based trap for peroxynitrite used to detect entry of peroxynitrite into erythrocyte ghosts. Macfadyen A J; **Reiter C**; Zhuang Y; Beckman J S. (Department of Pediatrics, Center for Free Radical Biology, University of Alabama at Birmingham, Birmingham, Alabama 35233, USA.) CHEMICAL RESEARCH IN TOXICOLOGY, (1999 Mar) 12 (3) 223-9. Journal code: 8807448. ISSN: 0893-228X. Pub. country: United States. Language: English.

L21 ANSWER 10 OF 68 MEDLINE DUPLICATE 3
1998018269 Document Number: 98018269. PubMed ID: 9378996. Depletion of CD8+ T lymphocytes by murine monoclonal CD8 **antibodies** and restored specific T cell proliferation in vivo in a patient with chronic hepatitis C. Kiefersauer S; **Reiter C**; Eisenburg J; Diepolder H M; Rieber E P; Riethmuller G; Gruber R. (Institute for Immunology, Klinikum Grosshadern, University of Munich, Germany.) JOURNAL OF IMMUNOLOGY, (1997 Oct 15) 159 (8) 4064-71. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

L21 ANSWER 11 OF 68 MEDLINE DUPLICATE 4
96225797 Document Number: 96225797. PubMed ID: 8642089. Treatment of severe cutaneous lupus erythematosus with a chimeric CD4 monoclonal **antibody**, cM-T412. Prinz J C; Meurer M; **Reiter C**; Rieber E P; Plewig G; Riethmuller G. (Department of Dermatology, Ludwig-Maximilians-University, Munich, FRG.) JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, (1996 Feb) 34 (2 Pt 1) 244-52. Journal code: 7907132. ISSN: 0190-9622. Pub. country: United States. Language: English.

L21 ANSWER 12 OF 68 MEDLINE DUPLICATE 5
96317110 Document Number: 96317110. PubMed ID: 8743291. Structural diversity of monoclonal CD4 **antibodies** and their capacity to block the HIV gp120/CD4 interaction. Weissenhorn W; Chen Y H; **Reiter C**; Federle C; Weiss E H; Riethmuller G; Rieber E P. (Institut fur Immunologie, Munchen, Germany.) HYBRIDOMA, (1996 Apr) 15 (2) 117-24. Journal code: 8202424. ISSN: 0272-457X. Pub. country: United States. Language: English.

L21 ANSWER 13 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1995:384458 Document No.: PREV199598398758. CD4, CD8 and CD 18 chimeric monoclonal **antibodies** (chim mAbs) with or without donor bone marrow transplantation for induction of tolerance after heart transplantation (HTx. Meiser, B. M.; Kreuzer, E.; **Reiter, C.**; Riethmueller, G.; Reichart, B.. Dep. Cardiac Surg., Inst. Immunol., Univ. Munich, Munich Germany. 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 650. The 9th International Congress of Immunology. Publisher: 9th International Congress of Immunology San Francisco, California, USA. Meeting Info.: Meeting Sponsored by the American Association of Immunologists and the International Union of Immunological Societies San Francisco, California, USA July 23-29, 1995 Language: English.

L21 ANSWER 14 OF 68 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
95259091 EMBASE Document No.: 1995259091. Restricted expression of the irreC-rst protein is required for normal axonal projections of columnar visual neurons. Schneider T.; **Reiter C.**; Eule E.; Bader B.; Lichte B.; Nie Z.; Schimansky T.; Ramos R.G.P.; Fischbach K.-F.. Institut fur Biologie III, Albert-Ludwigs-Universitat Freiburg,D-79104 Freiburg, Germany. Neuron 15/2 (259-271) 1995.
ISSN: 0896-6273. CODEN: NERNET. Pub. Country: United States. Language: English. Summary Language: English.

L21 ANSWER 15 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1995:150530 Document No.: PREV199598164830. CD4, CD8 and CD 18 chimeric monoclonal **antibodies** (chim mAbs) with or without donor bone marrow transplantation for induction of tolerance after heart transplantation (HTx. Meiser, B. M. (1); Kreuzer, E.; **Reiter, C.** ; Riethmueller, G.; Reichart, B.. (1) Dep. Cardiac Surg., Univ. Munich, Grosshadern Med. Center, 81366 Munich Germany. Journal of Heart and Lung Transplantation, (1995) Vol. 14, No. 1 PART 2, pp. S57. Meeting Info.: Fifteenth Annual Meeting and Scientific Sessions of the International Society for Heart and Lung Transplantation San Francisco, California, USA April 5-8, 1995 ISSN: 1053-2498. Language: English.

L21 ANSWER 16 OF 68 MEDLINE DUPLICATE 6
95204958 Document Number: 95204958. PubMed ID: 7897241. A novel non-radioactive cellular cytotoxicity test based on the differential assessment of living and killed target and effector cells. Flieger D; Gruber R; Schlimok G; **Reiter C**; Pantel K; Riethmuller G. (Institute for Immunology, University of Munich, Germany.) JOURNAL OF IMMUNOLOGICAL METHODS, (1995 Mar 13) 180 (1) 1-13. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

L21 ANSWER 17 OF 68 MEDLINE DUPLICATE 7

94353491 Document Number: 94353491. PubMed ID: 7915442. Chimeric monoclonal CD4 **antibody**--a novel immunosuppressant for clinical heart transplantation. Meiser B M; **Reiter C**; Reichenspurner H; Uberfuhr P; Kreuzer E; Rieber E P; Riethmuller G; Reichart B. (Department of Cardiac Surgery, Ludwig-Maximilians University of Munich, Germany.) TRANSPLANTATION, (1994 Aug 27) 58 (4) 419-23. Journal code: 0132144. ISSN: 0041-1337. Pub. country: United States. Language: English.

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L21 ANSWER 19 OF 68 MEDLINE DUPLICATE 9
94174238 Document Number: 94174238. PubMed ID: 8128188. Treatment of rheumatoid arthritis with a chimeric CD4 monoclonal **antibody** (cM-T412): immunopharmacological aspects and mechanisms of action. van der Lubbe P A; **Reiter C**; Miltenburg A M; Kruger K; de Ruyter A N; Rieber E P; Bijl J A; Riethmuller G; Breedveld F C. (Department of Rheumatology, University Hospital Leiden, The Netherlands.) SCANDINAVIAN JOURNAL OF IMMUNOLOGY, (1994 Mar) 39 (3) 286-94. Journal code: 0323767. ISSN: 0300-9475. Pub. country: ENGLAND: United Kingdom. Language: English.

L21 ANSWER 20 OF 68 MEDLINE DUPLICATE 10
94030111 Document Number: 94030111. PubMed ID: 8216397. Chimeric CD4 monoclonal **antibody** cM-T412 as a therapeutic approach to rheumatoid arthritis. van der Lubbe P A; **Reiter C**; Breedveld F C; Kruger K; Schattenkirchner M; Sanders M E; Riethmuller G. (Department of Rheumatology, University Hospital Leiden, The Netherlands.) ARTHRITIS AND RHEUMATISM, (1993 Oct) 36 (10) 1375-9. Journal code: 0370605. ISSN: 0004-3591. Pub. country: United States. Language: English.

L21 ANSWER 21 OF 68 MEDLINE DUPLICATE 11
93174759 Document Number: 93174759. PubMed ID: 8438481. Selection and chimerization of a monoclonal CD4 **antibody** for heart transplantation. **Reiter C**; Meiser B M; Uberfuhr P; Wenke K; Reichenspurner H; Kreuzer E; Rieber E P; Riethmuller G; Reichart B. (Department of Cardiac Surgery, Ludwig-Maximillians University of Munich, Germany.) TRANSPLANTATION PROCEEDINGS, (1993 Feb) 25 (1 Pt 1) 788-9. Journal code: 0243532. ISSN: 0041-1345. Pub. country: United States. Language: English.

L21 ANSWER 22 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 12
1993:333407 Document No.: PREV199345028132. CD4-**antibody** treatment of inflammatory bowel disease: One year follow up. Deusch, K.; Mauthe, B.; **Reiter, C.**; Riethmueller, G.; Classen, M.. II. Dep. Med., Technical Univ., Munich Germany. Gastroenterology, (1993) Vol. 104, No. 4 SUPPL., pp. A691. Meeting Info.: 94th Annual Meeting of the American Gastroenterological Association Boston, Massachusetts, USA May 15-21, 1993 ISSN: 0016-5085. Language: English.

L21 ANSWER 23 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
1993:538589 Document No.: PREV199345125683. Treatment of cutaneous lupus erythematosus with a chimeric monoclonal CD4 **antibody**. Prinz, J. C.; Meurer, M.; **Reiter, C.**; Plewig, G.; Riethmueller, G.. Dep. Dermatol., Inst. Immunol., Univ. Munich, 80337 Munich Germany. Journal of Investigative Dermatology, (1993) Vol. 101, No. 3, pp. 446. Meeting Info.: Second Tricontinental Meeting of the JSID (Japanese Society for

Investigative Dermatology), SID (Society for Investigative Dermatology, Inc.), and ESDR (European Society for Dermatological Research) Kyoto, Japan October 28-31, 1993 ISSN: 0022-202X. Language: English.

L21 ANSWER 24 OF 68 MEDLINE DUPLICATE 13
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L21 ANSWER 25 OF 68 MEDLINE DUPLICATE 14
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L21 ANSWER 26 OF 68 MEDLINE DUPLICATE 15
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